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High resolution metabolomics to identify novel biomarkers in corticosteroid resistant asthmatic children

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Corticosteroid (CS) treatment is the preferred anti-inflammatory treatment for adults and children with asthma. However, a subset of patients fails to respond to combined systemic and inhaled CS treatment despite very high doses and prolonged treatment. Due to the uncertainty of the molecular mechanism for CS-resistant asthma, this study is aimed at discovering diagnostic biomarkers for early identification of children resistant to CS. High resolution metabolomics (HRM) was performed on plasma and urine samples from CS-respondent and CS-non-respondent children to determine putative biomarkers related to CS resistance. The metabolic phenotypes of CS-responders and CS-non-responders were analyzed using bioinformatics including Manhattan plot with False Discovery Rate (FDR), Hierarchical Cluster Analysis (HCA), Kyoto Encyclopedia Genes and Genomes (KEGG) and Mummichog pathway analysis. The Manhattan plot with false discovery rate determined 1894 metabolites in plasma and 30 metabolites in urine significantly altered between CS-responders and CS-non-responders. The important metabolites annotated were S-adenosylmethionine (439.1395 *m/z*, $[M+ACN+H]^+$) and S-adenosylmethionine (378.1448 *m/z*, $[M+Na]^+$) in plasma as well as ϒ-glutamylcysteine (236.06 *m/z*, $[M+S(34)+H]^+$) and Cys-Gly, (253.06 *m/z*, $[M-NH_3+H]^+$), reduced FMN (517.0794 *m/z*, $[M+NaCl]^+$). Thus, the metabolites in glutathione metabolism were altered significantly regarding CS resistance. The identified biomarkers in urine of asthmatic children would be extremely beneficial not only for early detection, but also in the development of therapies aimed at preventing the irreversible airway damage and lung function decline associated with CS resistance in severe asthma among children.

Biography

Youngja H Park completed her MS and PhD in Pharmacology and Toxicology under Dr. James P Kehrer at University of Texas at Austin in 1990. She previously had worked as an Assistant Professor in the Department of Medicine and as the Assistant Director of the Clinical Biomarkers Laboratory at Emory University School of Medicine since 2013. At Emory University, she developed LC-MS based metabolomics pipelines to identify novel biomarkers and the pathways associated with diseases. She published number of metabolomics papers in *Science and Journal of Allergy and Clinical Immunology*. Currently, she moved back to College of Pharmacy, Korea University where she has built metabolomics core facility after years of experience in research, evaluation and teaching both in hospital and education institutions. Her career goal is to identify the novel biomarkers and develop the sensors in early diagnoses of disease.

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